Application No.: 10/613,524 9 Docket No.: C1037.70042US00

Reply to Office Action of June 27, 2007

### REMARKS

Applicant respectfully requests reconsideration.

Applicant has renumbered claims 17-99 to claims 16-98 to correct a typographical error in the previous claim numbering. The claim numbering referred to in this amendment is based on the corrected numbers.

Claims 1, 18-45 and 96-98 are amended. Support for the amendments to claim 1 can be found at least in originally filed claims 1, 17 and 18, and in the specification on page 4 lines 11-13 and page 14 lines 1-10. Claims 18-45 and 96-98 are amended to correct claim numbering and claim dependencies. Claims 18 and 19 are amended to depend from pending claim 1. Claims 28, 43 and 44 have been amended to correct their dependencies due to the change in claim numbering. Claim 22 is amended to recite "more than four CpG motifs". Support for this amendment can be found at least on page 11 lines 18-19 of the specification.

New claims 99-102 are added. Support for new claim 99 can be found in the specification at least on page 11 lines 15-16 and page 14 lines 1-10. Support for new claim 100 can be found at least in originally filed claims 1 and 3 and in the specification at least at page 14 lines 1-10. Support for new claim 101 can be found in the specification at least on page 15 line 28 and page 14 lines 1-10. Support for new claim 102 can be found at least in originally filed claims 1 and 2 and in the specification at least at page 14 lines 1-10.

Claims 16 and 17 are now cancelled.

Claims 1-45 and 96-98 were previously pending in this application. Claims 14, 15, 40-42, 45, and 96-98 are withdrawn. As a result, claims 1-13, 18-39, 43-44, and 99-102 are pending for examination with claims 1, and 99-102 being independent claims.

No new matter has been added.

## **Elections/Restrictions**

Applicant notes some ambiguity as to whether claims 12 and 13 are under examination. The Examiner has listed claims 12-15 as withdrawn, and claims 1-13 as rejected. Applicant believes that claims 12 and 13 are under examination. Clarification and/or confirmation is requested.

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### Information Disclosure Statement

The Examiner has indicated that the Information Disclosure Statement filed on March 21, 2005 fails to comply with the provisions of 37 CFR 1.97 and 1.98 and MPEP 609 because it lacked a column for the Examiner's initials. Applicant is resubmitting this Information Disclosure Statement with the same information, in an amended form, to contain a column for the Examiner's initials. Consideration of the documents cited therein is requested.

### Rejection under 35 U.S.C. §101

Claims 1, 2, 3 and 22-25 are rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter.

The Examiner alleges that the claimed invention is drawn to a product of nature. Without conceding the correctness of the rejection, Applicant has amended claim 1 to recite, in pertinent part, "wherein the immunostimulatory nucleic acid has a nucleotide backbone comprising at least one phosphorothioate modification." A nucleic acid with a phosphorothioate modification is not normally found in nature, and thus is eligible subject matter for patenting.

Reconsideration and withdrawal of this rejection is respectfully requested.

# Rejection under 35 U.S.C. §112, first paragraph

Claims 39 and 44 are rejected under 35 U.S.C. §112, first paragraph, enablement. The Examiner alleges that the specification does not reasonably provide enablement for a composition comprising the immunostimulatory nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 for treating or preventing an infectious disease or herpes simplex virus. More specifically, the rejection appears focused on the following issues: (a) the methylated or unmethylated status of the CpG motifs in the claimed nucleic acids, (b) the efficacy of the claimed nucleic acids for a range of infectious disease, (c) the efficacy of the claimed nucleic acids when used in the absence of antigen, (e) the safety of the claimed nucleic acids, and (f) supposed variability between CpG nucleic acids. At the outset, Applicant notes that the claims have been amended to recite that the cytosines of one or more of the four CpG motifs of the SEQ ID NO:1 is unmethylated. Applicant

otherwise respectfully traverses the rejection for the reasons set forth below which address each of the issues raised by the Examiner.

The enablement requirement is satisfied if one of ordinary skill in the art is able to make and use the claimed invention without undue experimentation, based on the specification and the knowledge in the art at the time of filing. The experimentation required to make and use the claimed invention may be complex, and still not undue, if the art routinely engages in that level of experimentation. The factors to be considered in determining whether undue experimentation is required include 1) the nature of the invention; 2) the breadth of the claims; 3) the state of the art; 4) the level of ordinary skill in the art; 5) the level of predictability in the art; 6) the amount of direction provided by the inventor(s); 7) the existence of working examples; and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731; 8 USPQ 2d 1400 (Fed. Cir. 1988). These factors are to be considered in their totality with no one factor being dispositive. The analysis of these factors as presented below illustrates that the experimentation required to practice the invention is not undue.

<u>Nature of the invention:</u> The invention relates to nucleic acids that comprise at a minimum a defined core 21 nucleotide sequence (i.e., SEQ ID NO:1). These nucleic acids are, by definition, immunostimulatory. They are able to stimulate an innate immune response as well as an adaptive immune response.

<u>Breadth of the claims:</u> The rejected claims relate to compositions of nucleic acids comprising the defined core nucleotide sequence (i.e., SEQ ID NO:1) in an amount effective to treat or prevent an infectious disease, such as herpes simplex virus infection.

State of the art and Predictability in the Art: The state of the art at the time of filing was aware of immunostimulatory nucleic acids, including CpG immunostimulatory nucleic acids. The immunostimulatory properties of a number of CpG nucleic acids were known at that time. (See, for example, USPs 6,194,388 and 6,207,646, issued prior to the effective filing date of the instant application and disclosing the ability of CpG nucleic acids to stimulate innate and antigen-specific immune responses.) This art disclosed the use of CpG nucleic acids in the treatment and/or prevention of infectious disease, including viral infectious disease. The art contemplated and described the use of CpG nucleic acids as monotherapy as well as in combination therapy (such as

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for example with antigen). It was known that CpG nucleic acids are able to stimulate immune responses including cytokine profiles and immune cell stimulation and/or activation profiles that are consistent with a Th1 immune response, which in turn was known to be useful in the treatment and/or prevention of infectious diseases. Thus, contrary to the Examiner's position, CpG nucleic acids are themselves immunostimulatory even in the absence of antigen. The examples provided in the instant specification attest to this fact.

The Examiner further states that "the scope of infectious disease is broad" as a basis for the rejection. The claimed nucleic acids stimulate a Th1-biased immune response that is known to treat infectious disease. Again, the art of record demonstrates that Th1-biased immune response induction is effective against infectious disease. (See for example Weiner et al. cited by the Examiner and discussed in greater detail below.) The Examples demonstrate the Th1-biased immune responses induced by the claimed nucleic acids.

The Examiner cites Choi et al., Vaccine 2002, 20:1733-1740 and Gallichan et al., J. Immunol 2001, 166 (5):3451-3457 in support of the proposition that CpG nucleic acids are effective in infectious disease when used as adjuvants but not when used in the absence of antigen. Applicant traverses the characterization of the reference teachings. Choi et al. does not even test CpG nucleic acids alone and the experiments of Gallichan et al. were not designed to test the efficacy of adjuvants when used alone. Rather the latter reference tested whether intranasal vaccination (with antigen and adjuvant) could impart protection at a distal mucosal site (i.e., the genital tract). That the single CpG nucleic acid used by Gallichan et al. did not impart such protection when administered alone intranasally does not establish that other CpG nucleic acids (including those of the pending claims which have more CpG motifs than does the oligonucleotide of Gallichan et al.) would not impart mucosal protection at a distal site or that it would not impart protection at all when used either mucosally or systemically. Moreover the pending claims are compositions, not methods of use, and as such they are not limited to any particular route of administration.

The Examiner cites Juffermans et al. Infect. Immun. 2002, 70(1):147-152 and Krieg et al. Abstract 1996 Meeting Molecular Approaches to the Control of Infectious Diseases, Sept. 9-Sept. 13, 1996 in support of the proposition that CpG oligonucleotides do not prevent disease due to an infection. However the Examiner also acknowledges that these references teach that

"immunostimulatory nucleic acids comprising unmethylated CpG dinucleotide when administered alone protect against infection with lethal L. monocytogenes or M. tuberculosis in a mice model". Juffermans et al. and Krieg et al. report the effects with a *single* dose of a *single* CpG oligonucleotide. The oligonucleotide of Juffermans et al. comprised a single CpG motif and it is to be distinguished from those of the pending claims which comprise at least four such motifs and two poly-T stretches. As evidence of the effect of multiple doses, Juffermans et al. report that two administrations of its particular CpG nucleic acid resulted in the survival of all treated mice at 4 months post-infection while 40% of control mice died during the same period. (See for example FIG. 4.) Juffermans et al. further report that CpG oligonucleotides administered at least 48 hours prior to L. monocytogenes infection provided protection. (See page 150, second column, Discussion.) When taken as a whole, Juffermans et al. and Krieg et al. stand for the proposition that CpG nucleic acids protect against M. tuberculosis and L. monocytogenes, respectively.

The Examiner cites Gramzinski et al. Infect. Immun. 2001 69:1643-1649 in support of the proposition that CpG nucleic acids do not prevent malaria infection. To the contrary, Gramzinski et al. demonstrate that a single dose of a single CpG nucleic acid induced protective immunity against P. yoelli infection. In particular, Table 1 documents that none of the ten mice administered a single dose of CpG nucleic acid 1 or 2 days before P. yoelli infection became infected whereas all ten of the control mice did. Gramzinski et al. also evidences that the protective effects of its CpG nucleic acid are dose dependent with higher doses resulting in greater protection. (See for example Table 2 which shows that 7 out of 10 mice administered 3 µg of CpG nucleic acid 7 days pre-infection became infected while only 2 out of 10 mice administered 100 µg of CpG nucleic acid became infected. The Table also shows that protection may also be dependent on timing of CpG nucleic acid administration since none of the mice given 50 µg of CpG nucleic acid at 2 days pre-infection became infected while 5 out of 10 treated at 7 days pre-infection became infected.)

The Examiner cites Gura Science 1995 270:575-577 for the proposition that CpG nucleic acid treatment might result in harmful side effects. The Gura reference refers to potentially toxic side effects associated with the use of oligonucleotides as antisense molecules. MPEP 2164.01(c) makes it clear that "the applicant need not demonstrate that the invention is completely safe." In fact, whether a pharmaceutical composition is safe for treating human subjects is within the domain

of the FDA, but not that of the PTO. In other words, safety is beyond the enablement standard as the law requires, and thus should not be a bar to patentability. *See* In re Brana, 51 F.3d 1560 (Fed. Cir. 1995). Notwithstanding this, Applicant notes that Several Phase I and II studies using CpG nucleic acids have demonstrated that the nucleic acids can be administered safely and are tolerated in humans. (See for example Kim et al., Blood, 104(11): abstract # 743, Nov. 16, 2004 (copy enclosed)).

The Examiner cites Weiner et al. J. Leukocyte Biology 2000 68:455-463, Ballas et al. J. Immunology 2001 167:4878-4886, and Agrawal et al. Trends in Molecular Medicine 2002 8(3):114-120 in support of the proposition that there is variability between CpG nucleic acids, between host species, and between cell types. With respect to all three references and the Examiner's concern about variability, Applicant notes that the claimed invention requires nucleic acids that share a 21 nucleotide core consensus sequence which imparts immunostimulatory activity. In other words, the claimed invention does not relate to *any* CpG nucleic acid, but rather a family of nucleic acids having at least a 21 nucleotide consensus sequence (i.e., SEQ ID NO:1) to which immunostimulatory activity is attributed. Secondly, the instant Examples show that the claimed nucleic acids stimulate mouse and human immune cells including B and NK cells, both of which are important in treating or preventing infectious disease.

Moreover Weiner et al. summarizes the immunostimulatory activity of CpG nucleic acids, and in doing so actually argues for, rather than against, predictability in the art. Weiner et al. discloses that CpG nucleic acids induce cytokines and activate immune cell subpopulations. The claimed nucleic acids possess similar immunostimulatory profiles as those described by Weiner et al., including B and NK cell activation, antibody secretion, IP-10 and IL-10 production, and IFN-  $\alpha$  secretion. Weiner et al. further teaches a correlation between the in vitro and in vivo immunostimulatory effects observed with CpG nucleic acids (see page 457, right column, third paragraph). Importantly, the reference also teaches the use of CpG nucleic acids in treatment of infectious disease. On page 458, left column, fourth paragraph, it states "Solid animal model data suggest the shift of the immune response to a Th1 response by CpG ODN could be of benefit for the treatment of infectious diseases by enhancing innate immunity or by serving as an immune adjuvant during vaccination." When taken as a whole, therefore, the reference supports predictability of

immunostimulation using CpG nucleic acids, especially in treating infectious disease. Ballas et al. relates to the anti-cancer effects of CpG nucleic acids. The rejected claims however relate to effective amounts for therapy of infectious disease and not cancer. And finally Agrawal et al. actually documents various studies in which CpG nucleic acids have been used as a monotherapy for infectious disease. (See Table 1) None of the references cited by the Examiner points to unpredictability in treating infectious disease using the claimed CpG nucleic acids.

The state of and level of predictability in the art at the effective filing date evidenced the use of CpG nucleic acids in the prevention and treatment of infectious disease. The Examiner has not provided any biological or immunological basis for why the claimed nucleic acids would not be effective against a broad range of infectious diseases.

<u>Level of ordinary skill in the art:</u> The person of ordinary skill in the art would be familiar with nucleic acid synthesis, formulation and administration in human or non-human subjects.

Amount of direction provided by the inventor(s): Applicant teaches how to make and use the claimed nucleic acids. The nucleotide sequence of SEQ ID NO:1 is provided. The art was familiar with how to make oligonucleotides comprising a defined sequence, and having a naturally occurring or modified backbone. In addition, the specification teaches de novo synthesis and/or modification of nucleic acids using any number of procedures. (See pages 17-23.) The art was also familiar with the ability of CpG nucleic acids to stimulate Th1-biased immune responses and therapeutic uses for such nucleic acids. In addition, the specification teaches the Th1-biased immune responses of the claimed nucleic acids. For in vivo use, the specification further teaches how to formulate, dose and administer the nucleic acids, and to whom to administer the nucleic acids. (See pages 81–89.)

<u>Working examples:</u> The Examiner asserts that "the specification teaches and provides guidance as to the *in vitro* ability of SEQ ID NO:1 (ODN 10103) to stimulate human PBMC, ... but does not provide guidance to the treatment or prevention of any infectious disease using an immunostimulatory nucleic acid comprising SEQ ID NO:1 by itself." The Examiner states "The specification does not correlate the clearing of infection e.g. herpes simplex virus with the administration of effective amounts of said immunostimulatory nucleic acid or compositions comprising such."

MPEP 2164.01(c) states "An *in vitro* or *in vivo* animal model example in the specification in effect constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention." The therapeutic efficacy of the claimed nucleic acids is attributable at least in part to their ability to stimulate Th1-biased immune responses. The Examples demonstrate Th1-biased immune induction by the claimed nucleic acids including induction of Th1 cytokines such as IFN-alpha, IP-10 and IL-10 by PBMC in vitro. Other Examples show the ability of the claimed nucleic acids to activate B cells in vitro as indicated by proliferation and surface marker activation, to induce NK lytic activity in vitro, and to stimulate antigen-specific antibody production in vivo when administered with an antigen. These Examples demonstrate that the claimed nucleic acids are capable of priming the immune system even in the absence of antigen. These Examples and the in vitro and in vivo activities they evidence are indeed working examples as they correlate with the contemplated in vivo use of the nucleic acids of the rejected claims.

The Examiner has not provided reasons for concluding a lack of correlation. According to the MPEP 2164.01(c), "the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable exact correlation is not required, as stated in Cross v. Iizuka, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985): Based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted)."

The Examiner cites Chatterjee et al. Cancer Immunol. Immunother., 1994, 38:75-82 in support of the proposition that "All of the art cited above were performed in animal models and it is art recognized that for any novel therapy, the transition from the laboratory to the clinic (Petri dish experiments to animal experiments to bedside) is a quantum leap." The relevance of the Chatterjee et al. reference is questionable for a number of reasons. First, the rejected claims are composition claims and their contemplated use is not limited to human subjects. Thus, even effects in non-human subjects are commensurate with the scope of the claims. Second, the therapy discussed by the reference is idiotypic antibody cancer immunotherapy which is clearly different from that of the instant claims. Third, the reference refers to "novel therapy" while in contrast, the use of CpG

nucleic acids generally for immune stimulation and specifically for treatment of conditions that benefit from such immune stimulation was known in the art at the time of filing. Finally, notwithstanding its Abstract, Chatterjee et al. concludes that "preliminary data and limited observations ... are encouraging and merit continuation ...".

Applicant has provided examples that the claimed nucleic acids are capable of stimulating immune responses in vivo and in vitro. These examples correlate with the scope of the rejected claims, and the specification therefore enables these claims. MPEP 2164.01(c).

Quantity of experimentation needed to practice the invention: In view of the teaching of the instant specification and the state of and level of predictability in the art at the time of filing, Applicant submits that the rejected claims can be practiced without undue experimentation.

Reconsideration and withdrawal of this rejection is respectfully requested.

### Rejection under 35 U.S.C. §102(e)

Claims 1, 22-25 and 34-35 are rejected under 35 U.S.C. §102(e) as being anticipated by Olek et al. WO 2002/00926 A2.

Without conceding the correctness of the rejection, Applicant has amended Claim 1 to recite, in pertinent part, "wherein the immunostimulatory nucleic acid has a nucleotide backbone comprising at least one phosphorothioate modification." Olek et al. does not teach phosphorothioate backbone modification of its nucleic acid sequences. Amended claim 1 finds its basis at least in originally filed claims 17 and 18 which were not rejected in view of Olek et al. New claim 100 finds its basis at least in originally filed claim 3 which also was not rejected in view of Olek et al. The nucleic acids of claims 99, 101 and 102 are not taught by Olek et al. and thus these claims are also not anticipated by Olek et al.

Reconsideration and withdrawal of this rejection is respectfully requested.

## Rejection under 35 U.S.C. §103(a)

Claims 1, 3-13, 16-38 and 43 are rejected under 35 U.S.C. §103(a) as being unpatentable over Olek et al. WO 2002/00926 A2 in view of Krieg et al. WO 2001/22972 A2.

The Examiner alleges that it would have been prima facie obvious to one of ordinary skill in the art to combine the teachings of Krieg et al. with the composition of Olek et al. The Examiner alleges that Olek et al. teaches a nucleic acid comprising the instantly claimed nucleic acid sequence, and Krieg et al. teaches phosphorothioate backbone modifications, and the addition of antigens, adjuvants, cytokines, anti-microbial agents, pharmaceutically acceptable carriers, and nucleic acids containing at least one unmethylated CpG dinucleotide.

Applicant respectfully traverses this rejection. MPEP 2143.01 IV states that "A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references. Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). Rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR, 550 U.S. at 14, 82 USPQ2d at 1396 quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

The teachings of Krieg et al. relate to the stimulation of an immune response. By contrast, Olek et al. teaches detection of the cytosine methylation status in chemically pretreated DNA, as well as a method for the diagnosis and/or therapy of conditions associated with (or without) this methylation status. Nowhere in the Olek et al. reference is there any suggestion to use its nucleic acids for induction of immune response. The aspects of the Krieg et al. reference which the Examiner relies upon, such as the phosphorothioate backbone modifications and the addition of antigens, adjuvants, cytokines, anti-microbial agents, pharmaceutically acceptable carriers, and nucleic acid containing at least one unmethylated CpG dinucleotide, all serve to induce, enhance, or vary an immune response. Since the Olek et al. reference does not relate to immune response induction, enhancement or variation, there would be no reason for one of skill in the art to combine the teachings of Krieg et al. with those of Olek et al. For at least this reason, the combination of references does not render obvious the rejected claims.

Reconsideration and withdrawal of this rejection is respectfully requested.

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# **CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: December 27, 2007

Respectfully submitted,

By HAYELL

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[743] TLR9 Agonist Immunomodulator Treatment of Cutaneous T-Cell Lymphoma (CTCL) with CPG7909. Session Type: Oral Session

Youn Kim, Michael Girardi, Madeline Duvic, Timothy Kuzel, Alain Rook, Brian Link, Lauren Pinter-Brown, Carol Comerci, Sonja McAuley, Tess Schmalbach. Dermatology, Stanford Medical Center, Palo Alto, CA, USA; Dermatology, Yale University School of Medicine, New Haven, CT, USA; Dermatology, MD Anderson Cancer Center, Houston, TX, USA; Hematology / Oncology, Northwestern University Medical Center, Chicago, IL, USA; Dermatology, University of Pennsylvania, Philadelphia, PA, USA; University of Iowa Hospitals and Clinics, Iowa City, IA, USA; Division of Hematology / Oncology, Olive View - UCLA Medical Center, Sylmar, CA, USA; Coley Pharmaceutical Group, Wellesley, MA, USA

CPG 7909 belongs to a new class of chemically defined CpG immunomodulators. that target dendritic cell TLR9 receptors inducing IL-12, IFN-gamma, and NK cell function. The rate and durability of response to CPG 7909 was investigated in refractory patients with recurrent or advanced CTCL, who had failed one or more systemic therapies. Dose escalation with weekly sc dosing of patients at 0.08. 0.16, 0.24, or 0.28 mg/kg (3 patients/cohort) for 24 weeks is nearing completion. Additional patients continue to receive treatment at 0.32 (4 patients) or 0.36 mg/kg (12 patients). Clinical response, monitored by Composite Assessment of Index Lesion Disease Severity (CA) and Physician's Global Assessment of Clinical Condition, has been documented. Of 28 patients enrolled, 7 (25%) have achieved objective clinical response, 5 with partial response (PR) and 2 with complete response (CR). Eleven patients have maintained stable disease (SD). while 10 have had progressive disease (PD). Eight patients have completed 24 weeks of treatment (5 SD, 2 PR, 1 CR) with 12-16 weeks of response while on study. Six patients (3 SD, 2 PR,1 CR) are currently ongoing in the study. Three patients (2 PR, 1 SD) continue to receive long term CPG 7909 at 0.12 mg/kg (58 total doses), 0.28 mg/kg (34 total doses) or 0.32 mg/kg (29 total doses) in a follow on protocol. Responses have been maintained up to 46 weeks. Weekly doses up to 0.36 mg/kg have been well tolerated. Most reported adverse events have been of CTC grade 1 or 2. The most common are dose-related local injection site reactions (erythema, induration, edema, inflammation and pain) and mild or moderate flu-like symptoms (fatigue, rigors, fever, arthralgia). Four patients had CTC grade 3 drug related AEs; one decreased lymphocyte count (0.08 mg/kg), one increased gamma glutamyl transferase (0.16 mg/kg), one decreased absolute polys (0.36 mg/kg) and one fatigue (0.36 mg/kg). Enrollment in the phase II portion of the study is ongoing and compares results of patients randomized to receive either 10 mg or 25 mg sc weekly for 24 weeks (equating to effective doses seen in dose escalation).

Clinical Response with CPG 7909 - 16 M, 12 F									
Dose	N	Disease Stage	CR	PR	SD	PD			
0.36 mg/kg	12	IB (7), IIB, III (3), IVA	0	2	6	4			

0.32 mg/kg	4	IIA, IIB, IVA (2)	1	0	1	2
0.28 mg/kg	3	IB (2), III	0	1	2	0
0.24 mg/kg	3	IB, IIB (2)	0	1	1	1
0.16 mg/kg	3	IB (2), IIA	1	1	1	0
0.08 mg/kg	3	IB (2), IVA	0	0	0	3
Total	28		7%	18%	39%	36%

Abstract #743 appears in Blood, Volume 104, issue 11, November 16, 2004 Keywords: Cancer immunotherapy|Phase II|Dendritic cell

Tuesday, December 7, 2004, 08:00 AM

Simultaneous Session: Lymphoma - Therapy with Biologic Agents (8:00 AM-10:00 AM)

# [743] TLR9 Agonist Immunomodulator Treatment of Cutaneous T-Cell Lymphoma (CTCL) with CPG7909. **Session Type: Oral Session**

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Date/Time: Tuesday, December 7, 2004 - 08:00 AM

Session Info: Simultaneous Session: Lymphoma - Therapy with

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